self-evident, and does not constitute the addition of new matter. Attached hereto as Appendix A is a marked-up version of amended claims 16, 18, 19, and 33 to show the changes made.

Restriction Requirement

The Office Action, on page 2, requires restriction to one of the following groups under 35 U.S.C. §121:

Group I: Claims 1-19 and 25-36, drawn to a recombinant bacterium expressing a cytokine and tumor antigen and method for use in cancer therapy, classified in class 424, subclass 93.2;

Group II: Claims 20-24, drawn to an E. coli-BCG shuttle plasmid, classified in class 534, subclass 320.1.

Applicants are required to elect one of the above groups for prosecution on the merits. The Examiner states that the inventions are distinct from each other because the methods appear to constitute patentably distinct inventions "because the bacteria of Group I do [not] require the use of a plasmid, much less the *E. coli*-BCG shuttle plasmid of Group II" and also "since not a single claim in Group I recites a plasmid or the claimed plasmid."

Applicants respectfully traverse the requirements for restriction, and submit that the requirement is improper.

First, in response to the comment from the Examiner that not a single claim in Group I recites a plasmid, Applicants point out that independent claims 17 and 19 each recite a plasmid.

Second, Applicants assert that the subject matter of these groups represent different embodiments of a single inventive concept for which a single patent should issue. The pending claims represent an intricate web of knowledge, continuity of effort, and consequences of a single invention, which merit examination of all of these claims in a single application. More particularly, all the claims are linked by a single, searchable, unifying aspect; *i.e.*, recombinant bacterium vaccines.

Third, Applicants submit that a sufficient search and examination with respect to the subject matter of all claims can be made without serious burden. As the M.P.E.P. states:

> If the search and examination of an entire application can be made without serious burden, the examiner must examine it on the merits, even though it includes claims to independent or distinct inventions.
>
> M.P.E.P. § 803 (7th ed., Rel. 78A, March 1999).

That is, even if the above-enumerated groups of claims are drawn to distinct inventions, the Examiner must still examine the entire application on the merits because doing so will not result in a serious burden.

Applicants submit that the search and examination of all the claims will have substantial overlap, (*e.g.*, a search for Group I will almost entirely encompass the search required for Group II) and no serious burden will result from searching and examining all claims in the same application. Therefore, the statement in the Office Action at page 2, second full paragraph, to the effect that the "search required for Group I is not required for Group II, and *vice versa*," is not accurate. Given the powerful computer-based search engines and data bases at the Examiner's disposal, Applicants submit that no serious burden will result from searching and examining all claims in the same application.

Therefore, in the interest of savings of time and cost to Applicants and the Patent Office, Applicants respectfully request that all the claims be searched and examined in a single application.

Nevertheless, in compliance with the directives in the Office Action and in order to expedite prosecution of the instant application, Applicants hereby elect, subject to the foregoing traverse, ***Group I, claims 1-19 and 25-36***, drawn to a recombinant bacterium expressing a cytokine and tumor antigen and method for use in cancer therapy.

SUMMARY

Applicants respectfully request entry of the above directed amendments into the application. If a telephone conversation with Applicants' attorney would help expedite the prosecution of the above-identified application, the Examiner is urged to call the undersigned attorney at (617) 227-7400.

Applicants believe no fee is due with this response. However, if a fee is due, please charge our Deposit Account No. 12-0080, under Order No. WII-014CP from which the undersigned is authorized to draw.

Dated: January 7, 2003

Respectfully submitted,

By _____

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APPENDIX A

Version with markings showing changes made to the amended claims:

16. (Amended) A recombinant mycobacterium comprising:

(a) a first DNA molecule encoding a Th1 cytokine;

(b) a first promoter;

(c) a mycobacterial secretion signal sequence;

(d) a second DNA molecule encoding a tumor antigen; and

(e) a second promoter;

wherein the 5' to 3' order is said first promoter of (b), said secretion signal sequence of (c), said first DNA molecule of (a), said second promoter of (e) and said second DNA molecule of (d), wherein the expression of said first DNA molecule of (a) is under the control of said first promoter of (b) and said cytokine is expressed and secreted from said mycobacterium and the expression of said second DNA molecule of (d) is under the control of said second promoter of (e) and said tumor antigen is expressed by said mycobacterium such that said recombinant mycobacterium is capable of inducing an immune response to said tumor antigen in a subject.

18. (Amended) A recombinant bacterium [encoding a tumor antigen and] having enhanced immunostimulatory properties comprising a first DNA molecule encoding a cytokine and a second DNA molecule encoding a tumor antigen, wherein said first DNA molecule encoding said cytokine is under the control of a first promoter and said cytokine is secreted from said bacterium in a biologically active form and wherein said second DNA molecule encoding said tumor antigen is under the control of a second promoter and said tumor antigen is expressed by said recombinant bacterium.

19. (Amended) A recombinant BCG [encoding MUC1 and] having enhanced immunostimulatory properties and having incorporated therein a plasmid comprising a first DNA

molecule encoding interleukin-2 operably linked to a first mycobacterial heat shock protein gene promoter and a mycobacterial secretion signal sequence and a second DNA molecule encoding MUC1 operably linked to a second mycobacterial heat shock protein gene promoter wherein the 5' to 3' order of said plasmid is said first promoter, said secretion signal sequence, said first DNA molecule encoding said interleukin-2 , said second promoter, said second DNA molecule encoding MUC1 wherein said interleukin-2 is expressed and secreted from said recombinant BCG in a biologically active form and said MUC1 is expressed by said recombinant BCG.

33. (Amended) A vaccine for immunizing a subject against a neoplastic disease, comprising a recombinant bacterium of any one of claims 1, 10, 16, 17, 18 or 19 and a pharmaceutically acceptable carrier therefor, wherein the recombinant bacterium is present in an amount effective to immunize a subject against a neoplastic disease.